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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,659	05/26/2006	Andrea Pastorello	50294/018001	5027
21559	7590	02/27/2009	EXAMINER	
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			KOSAR, AARON J	
			ART UNIT	PAPER NUMBER
			1651	
			NOTIFICATION DATE	DELIVERY MODE
			02/27/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

<i>Office Action Summary</i>	Application No.	Applicant(s)	
	10/580,659	PASTORELLO ET AL.	
	Examiner	Art Unit	
	AARON J. KOSAR	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2008.
2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17, 19-54, 61 and 63 is/are pending in the application.
4a) Of the above claim(s) 2, 7-13, 15, 25-31, 35, 36, 38, 40, 41 and 43 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1, 3-6, 14, 16, 17, 19-24, 32-34, 37, 39, 42, 44-53, 61 and 63 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4/03/2008</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's amendment and argument filed September 26, 2008 in response to the non-final rejection, are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Applicant has amended the claims by amending claims 1, 3, 14, 16, 19-21, 32-34, 37, 44, 45, and 53 and canceling claims 54-60, and 75-82. Claims 1-17, 19-54, 61, and 63 are pending of which claims 2, 7-13, 15, 25-31, 35, 36, 38, 40, 41, and 43 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected species, there being no allowable generic or linking claim. Claims 1, 3-6, 14, 16, 17, 19-24, 32-34, 37, 39, 42, 44-53, 61, and 63 are pending *and* have been examined on their merits to the extent the claims read on the elected species.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on April 3, 2008 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

*Claim Rejections - 35 USC § 112, ¶2*The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The claims are generally drawn to a multilayer composite material comprising a multicomponent inner-matrix composite material comprising a hyaluronic acid (HA) derivative and a matrix of bone/ceramic/demineralized bone, and further comprising an association with a hyaluronic acid (HA) derivative and at least one layer of a HA derivative.

Response to Arguments

Claims 19 and 20 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19 and 20 recite the term “the external layers” of claim 1. The claims remain indefinite, because the claims recite that the material comprises two or three layers respectively; however, the material of the external layers may be identical to the other external layers and also to the inner matrix layer (i.e. comprising a hyaluronic acid (or HA derivate)) and thus it is unclear how one would non-arbitrarily distinguish a composition as having a one layer versus two or more layers comprising the same material (i.e. a hyaluronic acid derivative), to the extent instantly claimed. Thus, it is unclear if the term “layers” in claims 19 and 20 is further descriptive of either of the recited terms in claim 1 or if the term “layers” describes a third element of the composition. Each is a reasonable interpretation of the claims and each embraces different subject matter such that one would not be apprised as to what Applicant intends to embrace by the claims, thereby rendering the claims indefinite.

*Claim Rejections - 35 USC § 103**Response to Arguments*

Applicant has argued that Valentini does not teach a multilayer composition, that coating does not embrace or teaches away from further layers, and that the instant invention embraces other forms than films; and that the prior art composition does not have use in bone regeneration/spinal surgery Applicant's arguments have been fully considered but, respectfully, they are found to be not persuasive.

In response to Applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a multilayer composition wherein the material/matrix comprising HA derivative precludes overlapping identity with the external layer comprising a HA derivative; excluding of film or porous scaffold composition or composition blends and coatings embraced by the prior art teachings) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicant's argument that the composition of Valentini does not have use in bone regeneration/spinal surgery, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. Since, absent objective evidence to the contrary and for the reasons of record, the prior art structure appears capable of performing the intended use, then it meets the claims.

Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

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Claims 1-17, 19-34, 37, 39, 42-53, 61, and 63 remain rejected under 35 U.S.C. 103(a) as being unpatentable over VALENTINI (US 5,939,323, of record).

The claims are generally drawn to a multilayer composition comprising an inner matrix of a hyaluronic acid (HA) derivative and a matrix in association with a hyaluronic acid derivative. The elected species are further drawn to an HA benzyl ester and tribasic calcium phosphate $[\text{Ca}_3(\text{PO}_4)_2]$.

VALENTINI teaches a composition comprising hyaluronic acid (HA) and derivatizing HA, including esterification of HA with uncharged organic groups, including benzyl groups, to decrease water solubility of the material. Valentini also beneficially teaches varying the degree of substitution on the hyaluronic acid backbone, including 100% esterification with benzyl-derivatized HA (e.g. column 1, ¶4; columns 4 and 5). The scaffold-forming composition may be further modified by combining the HA with a second phase, including hydroxyapatite or tricalcium phosphate (column 3, ¶3) and further including coating the composition with a second polymer (column 10, indent (2)(f)). The composition is provided in a three-dimensional biodegradable scaffold comprised of liner HA molecules (column 1, ¶4 and structure), which can be fabricated or trimmed into any size *and* shape *and* any pore size (column 2, ¶1; column 9, ¶2 and 6; column 13 line 1-3), including contacting with water/solvent.

A chemical is inseparable from its properties. Since the components taught by the prior art are disclosed by Valentini to function for the same purpose and to the extent as is instantly claimed/disclosed (i.e. as bone repair/substitute compositions); absent a definition of the minimum structural requirements defining the arrangement of compositions into species of forms including a sponge, (non)woven tissue, paste, granule, powder, etc. *and* absent objective evidence as to the criticality of the particular arrangement(s) of the composition components

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upon the functioning of the compositions to the extent claimed/disclosed, the compositions are deemed to still be obvious in view of the prior art compositions. As such, one may broadly and reasonably interpret the forms as compositions varying merely in linear dimensions and/or states of hydration and thus corresponding to the compositions made obvious by Valentini; and, thus Valentini constitutes a teaching that the claimed forms are within the purview of one of skill and would have been *prima facie* obvious to provide the composition in the form to the extent claimed for the same recited intended use(s).

It would have been obvious to vary the form of the composition, the percentage of derivatization in the HA derivative (i.e. varying the proportion of materials in the esterification of HA) because Valentini beneficially teaches that the composition may be trimmed and manipulated to attain the desired porous composition of the desired dimension and of any dimension (*any* size and shape). Valentini is relied upon for the reasons discussed above. If not expressly taught by Valentini, based upon the overall beneficial teaching provided by this reference with respect to the selection of and trimming to size of the composition in the manner disclosed therein, the adjustments of particular conventional working conditions (e.g., determining the ratio of components, determining one or more suitable size ranges in which to provide a composition, determining the drying time or contact time with solvent(s)), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Furthermore, it would have been obvious to further incorporate bioactive compounds into the composition, because Valentini beneficially teaches bioactive agents which are useful in the invention, including antibiotics, cytokines, molecules that effect cell migration, and bone

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morphogenic protein, among other compounds (Column 6, ¶1). One would have been motivated to incorporate said agents, because Valentini teaches that the agents are useful in the composition to promote ingrowth of the cells into the implantable material. One would have had a reasonable expectation of success in making a bioactive agent-supplemented composition, because the success of the composition depends merely upon the *contacting* of the primary HA composition scaffold with the agent and since the contacting may occur with the HA and the agent before or after scaffold formation and either within or upon the composition non-covalently or covalently (column 6, ¶4).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the reference(s), it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of objective evidence to the criticality of some undisclosed feature, side-by-side comparison(s), or objective evidence to the contrary.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AARON J. KOSAR whose telephone number is (571)270-3054. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday,EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sandra Saucier/
Primary Examiner, Art Unit 1651

/Aaron J Kosar/
Examiner, Art Unit 1651